REMARKS

Claims 54, 56, 60-64, 66, 67, 69, 72, 73 and 76-86 are pending. Claim 82 has been amended and the following remarks presented.

Claims 54, 56, 60-64, 66, 67, 69, 72, 73 and 76-86 were rejected under 35 USC 103(a) as being unpatentable over Casper et al in view of Fiedler et al and Ladner et al. The reasons for the rejection were essentially the same as given before. This rejection is respectfully traversed for substantially the same reasons given before, incorporated by reference here, and the following clarifying points.

The examiner maintains it obvious to modify the sequences to express the nucleic acid sequence in plants because Casper et al mention low yields in bacteria and mammalian cells while Fiedler et al mention higher yields when a nucleic acid encoding scFv is expressed in plants. The examiner contends one would be motivated by higher yields to express the recombinant gene in plants.

Yield is not the only concern. The only scFv produced in plants are not shown to have the claimed structural or biological properties. None of the references show that a plant can express a correctly folded scFv protein. Furthermore, there is no showing that the scFv produced by plants structurally mimics the natural immunoglobulins and likewise no showing of producing molecules able to elicit an immune response against the tumor.

The examiner is aware that animal cells glycosylate proteins differently from plant cells, and bacterial cells generally do not glycosylate proteins at all. Furthermore, different types of host cells fold, solubilize and compartmentalize a protein differently. The examiner contends that one could try to combine teachings using different types of host cells to express a gene. However this conclusion is based on a presumption that the expressed protein is the same. Such a presumption has repeatedly been shown to be false for many other proteins in the past. This rejection is merely "obvious to try" without expectation of producing the recited protein with all of its claimed features. This is not the standard for patentability.

Fiedler et al shows that the plant produced protein binds to certain organic chemicals (oxazolone or abscisic acid). This chemical property does not require the scFv to mimic the natural tumor antigen at all, much less elicit an immune response to tumor cells as a method for

treating cancer. Measuring one chemical binding property does not establish the structure of a molecule, particularly when the molecule produced in the invention does not have the same chemical binding property. For the present invention, the expressed protein must mimic natural protein to meet the claimed structural recitations, features neither mentioned by nor even implied by Fiedler et al.

As a separate issue, the examiner contends it obvious to use a linker. This is true. The next step is to use a library of linkers such as proposed by Ladner et al. This conclusion does not follow. Ladner et al teach merely how to find a specific linker based on extensive measurements. Ladner et al specifically teaches against using a randomized library of linkers by stating their method is much better, resulting in making only one optimal linker. The linkers used by Ladner et al and Tang et al are for bacterial expression of a protein, not expression in plants. The linker not only holds the two domains together, it is important for folding the protein correctly which affects the protein solubility in cell, preventing host cell denaturing, or degradation of the scFv (by cellular protease cleavage, etc), post translationally modification and perhaps secretion from or compartmentalization within cell. These structural properties of the molecule depend on the combination of linker and type of cell expressing the nucleic acid. The bacterial cells used as the host cells, which are very different from plant cells.

Also, claim 67 contains two recitations not mentioned by Ladner et al or Tang et al. Ladner is silent as to the specific sequences to be used and in any event does not teach using a library of any type of linkers. The randomized linker library in Tang et al always contains 54 nucleotides, encoding exactly 18 amino acids in size. Claims 67 and 77 recite that the "...randomized library of linkers that vary in size..." No size variation exists in Tang et al. Secondly, the 18 repeated triplets in Tang are each identified as SNN where S = A, G or C and N = A, T, G or C. The Tang linkers include sequences that violate the definitions of claims 67, 69, 77 and 78. These claims state that position 1 of each triplet cannot be the same as position 2, the statement that position 2 of the triplet cannot be the same as position 3 or the statement that position 1 of the triplet cannot be the same as position 3. Likewise, the recitations in claim 69 and 78 make requirements to the linker not taught by and are opposed by Tang et al. Ladner et al is even further away by not specifying any rules as to the composition of the linker other than that

optimized by extensive calculations. As such they teach a different linker or set of linkers from the claimed linkers, and consequently cannot suggest using these in the claimed polynucleotides.

As a separate issue, the examiner notes the general principle that claim features drawn to intended use of the product are not a patentable aspect to the product. However, the claimed recitations are more than intended use but rather limitations to the structure of the product. While an intended use is implied, these features require certain structural properties to the molecules in the claim.

The protein's three-dimensional configuration is at issue. One may readily produce a protein by s similar method, which chemically appears the same but is a denatured or insolubilized protein, a degraded protein cleaved by the host cells proteases or a protein differently post translationally modified. All of these results are common when producing a protein in a foreign cell recombinantly. The resulting protein may have at least part of the amino acid sequence in common but the composition may be quite different structurally and functionally. In the present invention, the three-dimensional folding to correctly position the linked domains to mimic the natural tumor antigen is essential. The claims recite that the protein is obtainable from plant cells in correctly folded form to mimic he epitopes in their native form, the protein induces an immune response in a mammal and the protein includes the unique tumor epitope which distinguishes that tumor from others.

Fiedler et al shows plant produced scFv have a different property, chemical binding, which may still be accomplished by a scFv which is denatured, cleaved or post translationally modified. There is no suggestion that the Fiedler et al scFv mimic a tumor antigen in any way to meet the claimed recited structural requirements. The other references are even further away from the structural recitations because these references use entirely different host expression systems, which even if they produced the same protein would not establish that a plant could do so also.

Since none of the references alone or in combination teach a polynucleotide sequence capable of being expressed in plants to produce the recited protein (with the claimed structure), the rejection should be withdrawn.

In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested. If any issues remain, the examiner is encouraged to telephone the undersigned.

If needed, applicants petition for an extension of time under the provisions of 37 CFR 1.136(a) for sufficient time to accept this response. The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No. 500933.

Respectfully submitted,

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Attachment: Petition for a three-month extension of time

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